

REMARKS

Upon entry of the present amendment, claims 1-3, 5-8,10-11, and 13-26 will remain pending in the above identified application, with claims 21-26 standing ready for further action on the merits, and claims 1-3,5-8, 10-11 and 13-20 standing withdrawn from further consideration on the merits based on an earlier restriction requirement of the Examiner.

The amendments made herein to the claims do not incorporate new matter into the application as originally filed. For example, newly added claim 26 finds in the specification at page 18, line 23 to page 19, line 10. Also, the amendments to claims 21-25 simply correct minor typographical errors (see claim 25), and/or clarify the language of the claims by replacing BCG-CWS with "Bacillus Calmette-Guerin cell wall skeleton" (see claims 21, 23 and 24), and/or clarify that the "dispersion-aiding solvent" is "an organic-solvent" (see claims 21-22), and/or put the claims into better condition for purposes of issuance in a United States Patent, by more distinctly setting forth the invention that the Inventors regard as their own.

The specification has also been amended to capitalize certain trademarks used therein.

Restriction Requirement

Applicants acknowledge their prior election with traverse to prosecute the invention of Group IV (claims 21-25). It is submitted that no undue burden would be placed on the Examiner to consider each of the pending claims 1-3, 5-8,10-11, and 13-26 at present, so that withdraw of the prior restriction is requested at present.

Specification Objection

The Examiner has objected to the specification for using certain trademarks therein without providing the same in capital letters. Withdraw of the objection is respectfully requested based on the amendment made herein to the specification.

Claim Objections

The Examiner has objected to claims 21 and 25 as containing certain informalities therein. The claims have been amended in a fashion that removes the informalities noted by the Examiner.

Claim Rejections - 35 USC § 112, 2nd Paragraph

Each of claims 21-25 has been rejected under the provisions of 35 USC § 112, 2nd paragraph. Reconsideration and withdraw of the rejections are respectfully requested based on the following considerations.

The terms "obtainable" and "dispersion-aiding" have been removed from the claims. Further, the claims under consideration at present (claims 21-26) particularly and distinctly set forth the invention that the Inventors regard as their own, the statute requires no more.

Claim Rejections Under 35 USC § 102(b)/102(e)

Claims 21 and 23-25 have been rejected under the provisions of 35 USC § 102(b) as anticipated by Yamamura et al. (US 4,543,253), or Cantrell (US 4,877,611), or Yarkoni et al. (*Infection and Immunity*, 28(3):881-886 (1980)). Claims 21 and 23-25 have also been rejected under the provisions of 35 USC § 102(e) as anticipated by Van Nest et al. (US 6,451,325 B1). Reconsideration and withdraw of these rejections are respectfully requested based on the following considerations.

Oil-in-Water Emulsions of the Present Invention

The oil-in-water emulsion according to amended claim 21 is defined by the properties exhibited in the emulsion, and the process of the preparation of the emulsion, the properties being:

- 1) that the emulsion is negative for agglutination reaction with lectin;
- 2) that a BCG-CWS is encapsulated in an oil to form oil droplets; and

3) that the particle diameter of the oil droplets is 100 μm or less;
and the process comprising steps (a), (b) and (c) as indicated in amended claim 21.

When a BCG-CWS is dispersed without any organic solvent, then a particle diameter of the BCG-CWS should exceed 100 μm in size. Prior to the present invention, there was no dispersion comprising a BCG-CWS that was prepared with an organic solvent, i.e., a BCG-CWS having a particle diameter of about 100 μm or less, and therefore the invention of the present application is novel.

Distinctions Over the Cited Art

Yamamura et al. (US 4,543,253) describes compositions comprising *Nocardia rubra* cell wall skeleton. The present claims under consideration no longer recite *Nocardia rubra* cell wall skeleton.

Cantrell (US 4,877,611) describes vaccines comprising BCG-CWS. The Yarkoni et al. reference describes oil-in-water emulsions comprising BCG-CWS. However, no organic solvent is used to prepare vaccines or emulsions in the cited reference. As fully discussed hereinafter, the preparation without any organic solvent results in compositions different from the present invention.

Van Nest et al. (US 6,451,325 B1) describes adjuvant compositions comprising a metabolizable oil and an emulsifying

agent, the USPTO contends in the Office Action that Van Nest et al. teach that the composition comprises cell wall skeleton from Mycobacteria (col. 9, lines 8-15). However, Van Nest et al. do not describe any specific composition comprising BCG-CWS.

Further, Van Nest et al. do not describe any composition that comprises an organic solvent such as ethanol. The USPTO contends in the Office Action that Van Nest et al. teach that emulsifying agents include ethanol (col. 10, lines 58-63). However, that is incorrect. There is no word "emulsifying agents" in column 10, and ethanol recited in column 10 is described to be able to esterify an optionally esterified carboxyl group positioned on a preferred glycopeptide of Formula II, which stimulates an immune response. Thus, no organic solvent is used to prepare the compositions in Van Nest et al. As fully discussed hereinafter, the preparation without any organic solvent results in compositions different from the present invention.

Patentability of the Present Invention

In relation to every cited reference, in the Office Action it is stated that claim limitations such as "wherein the emulsion is negative for agglutination reaction with lectin", "having an particle diameter of about 100 μm or less is homogeneously dispersed" and "wherein the particle diameter is about 25 μm " would be inherent in the teachings of the prior art.

However, the USPTO misunderstands the technical features of the present invention, especially the effects of "an organic solvent" as used during the preparation of emulsions.

As shown in amended claim 21, an organic solvent is used to mix BCG-CWS and oil, and then the organic solvent is evaporated off to give an intended emulsion. In order to demonstrate the difference in particle size between with and without an organic solvent, a 37 CFR § 1.132 Declaration of Dr. Nomura is enclosed with the present response, and there is also enclosed second 37 CFR § 1.132 Declaration of Dr. Kawabe. The Examiner is respectfully requested to review the enclosed declarations of Dr. Nomura and Dr. Kawabe at present as the same contain comparative testing results that are probative of the patentability of each of the pending claims under consideration.

Upon review of the Dr. Nomura declaration, e.g., at page 5, the Examiner will see that Experiments 1(a) and 1(b) fine homogenous microparticles were obtained, whereas in Experiment 2 gave a mixture of particles having a large particle size. As indicated at page 2 of the declaration, "the comparative experiment was carried out to demonstrate the difference in particle size of the particle of BCG-CWS when a dispersion-aiding solvent is used or not."

Upon review of the Dr. Kawabe declaration, for example at page 2, the Examiner will see that comparative testing has been carried

out to "demonstrate that the morphology of BCG-CWS treated with an organic solvent is quite different from that of BCG-CWS treated with a physiological saline as commonly used" in the art.

As discussed above, and as shown in the accompanying 37 CFR 1.132 Declarations of Dr. Nomura and Dr. Kawabe, no cited reference describes, teaches or otherwise provides for the instant invention as claimed, and at the cited art in no way renders obvious the unexpected results that are associated with the invention, resulting from the use of organic solvent in preparation of the composition comprising BCG-CWS.

CONCLUSION

Based on the amendments and remarks presented herein, as well as the submission of Dr. Nomura's enclosed declaration and Dr. Kawabe's enclosed declaration, it is submitted that each of the pending claims under consideration is allowable at present. Accordingly, the Examiner is respectfully requested to issue a notice of allowance at present indicating the allowability of each of pending claims 21-26.

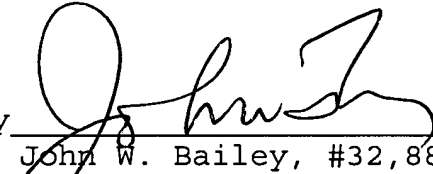
Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact John W. Bailey (Reg. No. 32,881) at the telephone number of the undersigned below, to conduct an interview

in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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By 
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JWB:enm
0020-4802P

Attachment(s): 37 CFR § 1.132 Declaration of Dr. Nomura
37 CFR § 1.132 Declaration of Dr. Kawabe

(Rev. 02/12/2004)